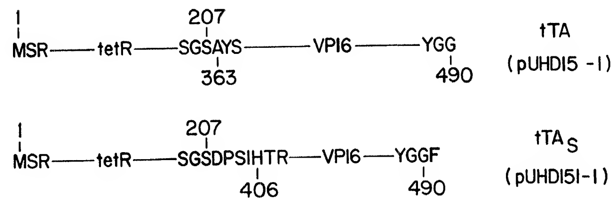

1
MSR—tetR—SGSAYS—VP16—YGG
207
363
490
tTA
(pUHD15 -1)
1
MSR—tetR—SGSDPSIHTR—VP16—YGGF
207
406
490
tTAS
(pUHD151-1)

FIG. 1A

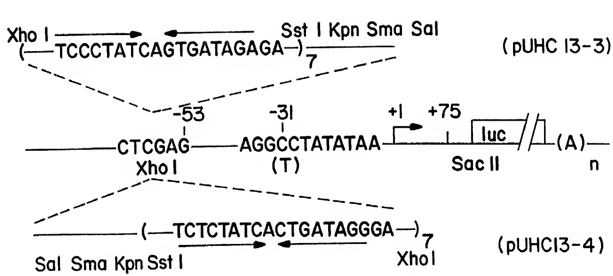

Xho I
(—TCCCTATCAGTGATAGAGA—)7
Sst I Kpn Sma Sal
(pUHC 13-3)
—CTCGAG—AGGCCTATATAA
Xho I
-53
-31
(T)
+1
+75
luc
Sac II
(A)n
(—TCTCTATCACTGATAGGGA—)7
Sal Sma Kpn Sst I
Xho I
(pUHC13-4)

FIG. 1B

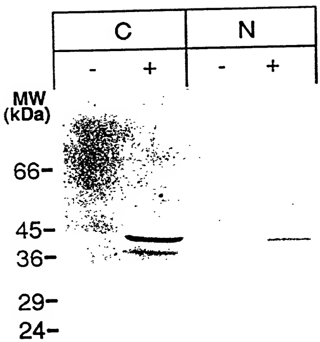


FIG. 2A

FIG. 2B

FIG. 3A

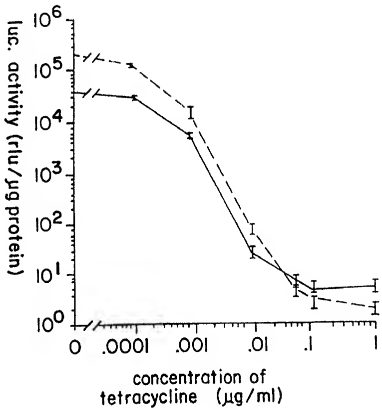
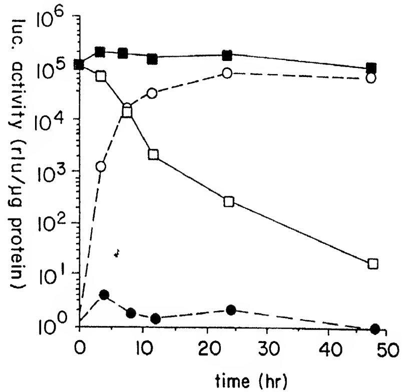

luc. activity (rlu/µg protein)
10^6
10^5
10^4
10^3
10^2
10^1
10^0
0
.0001
.001
.01
.1
1
concentration of tetracycline (µg/ml)

FIG. 3B


luc. activity (rlu/µg protein)
10^6
10^5
10^4
10^3
10^2
10^1
10^0
0
10
20
30
40
50
time (hr)

ATG TCT AGA TTA GAT AAA AGT AAA GTG ATT AAC AGC GCA TTA GAG CTG CTT AAT
Met Ser Arg Leu Asp Lys Ser Lys Val Ile Asn Ser Ala Leu Glu Leu Leu Asn

GAG GTC GGA ATC GAA GGT TTA ACA ACC CGT AAA CTC GCC CAG AAG CTA GGT GTA
Glu Val Gly Ile Glu Gly Leu Thr Thr Arg Lys Leu Ala Gln Lys Leu Gly Val

GAG CAG CCT ACA TTG TAT TGG CAT GTA AAA AAT AAG CGG GCT TTG CTC GAC GCC
Glu Gln Pro Thr Leu Tyr Trp His Val Lys Asn Lys Arg Ala Leu Leu Asp Ala

TTA GCC ATT GAG ATG TTA GAT AGG CAC CAT ACT CAC TTT TGC CCT TTA GAA GGG
Leu Ala Ile Glu Met Leu Asp Arg His His Thr His Phe Cys Pro Leu Glu Gly

GAA AGC TGG CAA GAT TTT TTA CGT AAT AAG GCT AAA AGT TTT AGA TGT GCT TTA
Glu Ser Trp Gln Asp Phe Leu Arg Asn Lys Ala Lys Ser Phe Arg Cys Ala Leu

Fig. 4A

CTA AGT CAT CGC GAT GGA GCA AAA GTA CAT TTA GGT ACA CGG CCT ACA GAA AAA
Leu Ser His Arg Asp Gly Ala Lys Val His Leu Gly Thr Arg Pro Thr Glu Lys

CAG TAT GAA ACT CTC GAA AAT CAA TTA GCC TTT TTA TGC CAA CAA GGT TTT TCA
Gln Tyr Glu Thr Leu Glu Asn Gln Leu Ala Phe Leu Cys Gln Gln Gly Phe Ser

CTA GAG AAT GCA TTA TAT GCA CTC AGC GCT GTG GGG CAT TTT ACT TTA GGT TGC
Leu Glu Asn Ala Leu Tyr Ala Leu Ser Ala Val Gly His Phe Thr Leu Gly Cys

GTA TTG GAA GAT CAA GAG CAT CAA GTC GCT AAA GAA GAA AGG GAA ACA CCT ACT
Val Leu Glu Asp Gln Glu His Gln Val Ala Lys Glu Glu Arg Glu Thr Pro Thr

ACT GAT AGT ATG CCG CCA TTA TTA CGA CAA GCT ATC GAA TTA TTT GAT CAC CAA
Thr Asp Ser Met Pro Pro Leu Leu Arg Gln Ala Ile Glu Leu Phe Asp His Gln

Fig. 4B

GGT GCA GAG CCA GCC TTC TTA TTC GGC CTT GAA TTG ATC ATA TGC GGA TTA GAA
Gly Ala Glu Pro Ala Phe Leu Phe Gly Leu Glu Leu Ile Ile Cys Gly Leu Glu

AAA CAA CTT AAA TGT GAA AGT GGG TCC GCG TAC AGC CGC GCG CGT ACG AAA AAC
Lys Gln Leu Lys Cys Glu Ser Gly Ser Ala Tyr Ser Arg Ala Arg Thr Lys Asn

AAT TAC GGG TCT ACC ATC GAG GGC CTG CTC GAT CTC CCG GAC GAC GAC GCC CCC
Asn Tyr Gly Ser Thr Ile Glu Gly Leu Leu Asp Leu Pro Asp Asp Asp Ala Pro

GAA GAG GCG GGG CTG GCG GCT CCG CGC CTG TCC TTT CTC CCC GCG GGA CAC ACG
Glu Glu Ala Gly Leu Ala Ala Pro Arg Leu Ser Phe Leu Pro Ala Gly His Thr

CGC AGA CTG TCG ACG GCC CCC CCG ACC GAT GTC AGC CTG GGG GAC GAG CTC CAC
Arg Arg Leu Ser Thr Ala Pro Pro Thr Asp Val Ser Leu Gly Asp Glu Leu His

Fig. 4C

```
TTA GAC GGC GAG GAC GTG GCG ATG GCG CAT GCC GAC GCG CTA GAC GAT TTC GAT
Leu Asp Gly Glu Asp Val Ala Met Ala His Ala Asp Ala Leu Asp Asp Phe Asp

CTG GAC ATG TTG GGG GAC GGG GAT TCC CCG GGT CCG GGA TTT ACC CCC CAC GAC
Leu Asp Met Leu Gly Asp Gly Asp Ser Pro Gly Pro Gly Phe Thr Pro His Asp

TCC GCC CCC TAC GGC GCT CTG GAT ATG GCC GAC TTC GAG TTT GAG CAG ATG TTT
Ser Ala Pro Tyr Gly Ala Leu Asp Met Ala Asp Phe Glu Phe Glu Gln Met Phe

ACC GAT CCC CTT GGA ATT GAC GAG TAC GGT GGG TAG
Thr Asp Pro Leu Gly Ile Asp Glu Tyr Gly Gly  *
```

Fig. 4D

ATG TCT AGA TTA GAT AAA AGT AAA GTG ATT AAC AGC GCA TTA GAG CTG CTT AAT
Met Ser Arg Leu Asp Lys Ser Lys Val Ile Asn Ser Ala Leu Glu Leu Leu Asn

GAG GTC GGA ATC GAA GGT TTA ACA ACC CGT AAA CTC GCC CAG AAG CTA GGT GTA
Glu Val Gly Ile Glu Gly Leu Thr Thr Arg Lys Leu Ala Gln Lys Leu Gly Val

GAG CAG CCT ACA TTG TAT TGG CAT GTA AAA AAT AAG CGG GCT TTG CTC GAC GCC
Glu Gln Pro Thr Leu Tyr Trp His Val Lys Asn Lys Arg Ala Leu Leu Asp Ala

TTA GCC ATT GAG ATG TTA GAT AGG CAC CAT ACT CAC TTT TGC CCT TTA GAA GGG
Leu Ala Ile Glu Met Leu Asp Arg His His Thr His Phe Cys Pro Leu Glu Gly

GAA AGC TGG CAA GAT TTT TTA CGT AAT AAC GCT AAA AGT TTT AGA TGT GCT TTA
Glu Ser Trp Gln Asp Phe Leu Arg Asn Asn Ala Lys Ser Phe Arg Cys Ala Leu

Fig. 5A

CTA AGT CAT CGC GAT GGA GCA AAA GTA CAT TTA GGT ACA CGG CCT ACA GAA AAA
Leu Ser His Arg Asp Gly Ala Lys Val His Leu Gly Thr Arg Pro Thr Glu Lys

CAG TAT GAA ACT CTC GAA AAT CAA TTA GCC TTT TTA TGC CAA CAA GGT TTT TCA
Gln Tyr Glu Thr Leu Glu Asn Gln Leu Ala Phe Leu Cys Gln Gln Gly Phe Ser

CTA GAG AAT GCA TTA TAT GCA CTC AGC GCT GTG GGG CAT TTT ACT TTA GGT TGC
Leu Glu Asn Ala Leu Tyr Ala Leu Ser Ala Val Gly His Phe Thr Leu Gly Cys

GTA TTG GAA GAT CAA GAG CAT CAA GTC GCT AAA GAA GAA AGG GAA ACA CCT ACT
Val Leu Glu Asp Gln Glu His Gln Val Ala Lys Glu Glu Arg Glu Thr Pro Thr

ACT GAT AGT ATG CCG CCA TTA TTA CGA CAA GCT ATC GAA TTA TTT GAT CAC CAA
Thr Asp Ser Met Pro Pro Leu Leu Arg Gln Ala Ile Glu Leu Phe Asp His Gln

Fig. 5B

```
GGT GCA GAG CCA GCC TTC TTA TTC GGC CTT GAA TTG ATC ATA TGC GGA TTA GAA
Gly Ala Glu Pro Ala Phe Leu Phe Gly Leu Glu Leu Ile Ile Cys Gly Leu Glu

AAA CAA CTT AAA TGT GAA AGT GGG TCT GAT CCA TCG ATA CAC ACG CGC AGA CTG
Lys Gln Leu Lys Cys Glu Ser Gly Ser Asp Pro Ser Ile His Thr Arg Arg Leu

TCG ACG GCC CCC CCG ACC GAT GTC AGC CTG GGG GAC GAG CTC CAC TTA GAC GGC
Ser Thr Ala Pro Pro Thr Asp Val Ser Leu Gly Asp Glu Leu His Leu Asp Gly

GAG GAC GTG GCG ATG GCG CAT GCC GAC GCG CTA GAC GAT TTC GAT CTG GAC ATG
Glu Asp Val Ala Met Ala His Ala Asp Ala Leu Asp Asp Phe Asp Leu Asp Met

TTG GGG GAC GGG GAT TCC CCG GGT CCG GGA TTT ACC CCC CAC GAC TCC GCC CCC
Leu Gly Asp Gly Asp Ser Pro Gly Pro Gly Phe Thr Pro His Asp Ser Ala Pro
```

Fig. 5C

```
TAC GGC GCT CTG GAT ATG GCC GAC TTC GAG TTT GAG CAG ATG TTT ACC GAT GCC
Tyr Gly Ala Leu Asp Met Ala Asp Phe Glu Phe Glu Gln Met Phe Thr Asp Ala

CTT GGA ATT GAC GAG TAC GGT GGG TTC TAG
Leu Gly Ile Asp Glu Tyr Gly Gly Phe  *
```

Fig 5D

GAATTCCTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTC

CCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGT

GAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCC

TATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGA

AAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGCTCGGTACCCGGGT

CGAGTAGGCGTGTACGGTGGGAGGCC<u>TATATAA</u>GCAGAGCTCGTTTAGTGAACCGTCAGATCGC

CTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGC

GG

Fig. 6

GAATTCCTCGACCCGGGTACCGAGCTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTA

AACTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCT

ATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAA

CTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTAT

CACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACT

CGAGTAGGCGTGTACGGTGGGAGGCCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGC

CTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGC

GG

Fig. 7

GAGCTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTC

TATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAA

ACTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTA

TCACTGATAGGGAGTGGTAAACTCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAAC

TCGACTTTCACTTTTCTCTATCACTGATAGGGAGTGGTAAACTCGAGATCCGGCGAATTCGAAC

ACGCAGATGCAGTCGGGGCGGCGCGGTCCGAGGTCCACTTCGCATATTAAGGTGACGCGTGTGG

CCTCGAACACCGAG

Fig. 8

CTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATC

AGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGT

CGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAG

TGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCG

AGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGCTCGGTACCCGGGTCGAGTA

GGCGTGTACGGTGGGAGGCCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCCTGGAG

ACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGCGGCCCC

GAATTCGAGCTCGGTACCGGGCCCCCCCTCGAGGTCGACGGTATCGATAAGCTTGATATCGAAT

TCCAGGAGGTGGAGATCCGCGGTCCAGCCAAACCCCACACCCATTTTCTCCTCCCTCTGCCCC

TATATCCCGGCACCCCCTCCTCCTAGCCCTTTCCCTCCTCCCGAGAGACGGGGGAGGAGAAAAG

GGGAGTT('AGGTCGACATGACTGAGCTGAAGGCAAAGGAACCTCGGGCTCCCCACGTGGCGGGC

GGCGCGCCCTCCCCCACCGAGGTCGGATCCCAGCTCCTGGGTCGCCCGGACCCTGGCCCCTTCC

AGGGGAGCCAGACCTCAGAGGCCTCGTCTGTAGTCTCCGCCATCCCCATCTCCCTGGACGGGTT

Fig. 9A

GCTCTTCCCCCGGCCCTGTCAGGGGCAGAACCCCCCAGACGGGAAGACGCAGGACCCACCGTCG

TTGTCAGACGTGGAGGGCGCATTTCCTGGAGTCGAAGCCCCGGAGGGGGCAGGAGACAGCAGCT

CGAGACCTCCAGAAAAGGACAGCGGCCTGCTGGACAGTGTCCTCGACACGCTCCTGGCGCCCTC

GGGTCCCGGGCAGAGCCACGCCAGCCCTGCCACCTGCGAGGCCATCAGCCCGTGGTGCCTGTTT

GGCCCCGACCTTCCCGAAGACCCCCGGGCTGCCCCCGCTACCAAAGGGGTGTTGGCCCCGCTCA

TGAGCCGACCCGAGGACAAGGCAGGCGACAGCTCTGGGACGGCAGCGGCCCACAAGGTGCTGCC

CAGGGGACTGTCACCATCCAGGCAGCTGCTGCTCCCCTCCTCTGGGAGCCCTCACTGGCCGGCA

GTGAAGCCATCCCCGCAGCCCGCTGCGGTGCAGGTAGACGAGGAGGACAGCTCCGAATCCGAGG

GCACCGTGGGCCCGCTCCTGAAGGGCCAACCTCGGGCACTGGGAGGCACGGCGGCCGGAGGAGG

AGCTGCCCCCGTCGCGTCTGGAGCGGCCGCAGGAGGCGTCGCCCTTGTCCCCAAGGAAGATTCT

CGCTTCTCGGCGCCCAGGGTCTCCTTGGCGGAGCAGGACGCGCCGGTGGCGCCTGGGCGCTCCC

CGCTGGCCACCTCGGTGGTGGATTTCATCCACGTGCCCATCCTGCCTCTCAACCACGCTTTCCT

GGCCACCCGCACCAGGCAGCTGCTGGAGGGGGAGAGCTACGACGGCGGGGCCGCGGCCGCCAGC

Fig. 9B

CCCTTCGTCCCGCAGCGGGGCTCCCCTCTGCCTCGTCCACCCCTGTGGCGGCGGCGACTTCC

CCGACTGCACCTACCCGCCCGACGCCGAGCCCAAAGATGACGCGTTCCCCCTCTACGGCGACTT

CCAGCCGCCCGCCCTCAAGATAAAGGAGGAGGAAGAAGCCGCCGAGGCCGCGGCGCGCTCCCCG

CGTACGTACCTGGTGGCTGGTGCAAACCCCGCCGCCTTCCCGGACTTCCAGCTGGCAGCGCCGC

CGCCACCCTCGCTGCCGCCTCGAGTGCCCTCGTCCAGACCCGGGGAAGCGGCGGTGGCGGCCTC

CCCAGGCAGTGCCTCCGTCTCCTCCTCGTCCTCGTCGGGGTCGACCCTGGAGTGCATCCTGTAC

AAGGCAGAAGGCGCGCCGCCCCAGCAGGGCCCCTTCGCGCCGCTGCCCTGCAAGCCTCCGGGCG

CCGGCGCCTGCCTGCTCCCGCGGACGGCCTGCCCTCCACCTCCGCCTCGGGCGCAGCCGCCGG

GGCCGCCCCTGCGCTCTACCCGACGCTCGGCCTCAACGGACTCCCGCAACTCGGCTACCAGGCC

GCCGTGCTCAAGGAGGGCCTGCCGCAGGTCTACACGCCCTATCTCAACTACCTGAGGCCGGATT

CAGAAGCCAGTCAGAGCCCACAGTACAGCTTCGAGTCACTACCTCAGAAGATTTGTTTGATCTG

TGGGGATGAAGCATCAGGCTGTCATTATGGTGTCCTCACCTGTGGGAGCTGTAAGGTCTTCTTT

AAAAGGGCAATGGAAGGGCAGCATAACTATTTATGTGCTGGAAGAAATGACTGCATTGTTGATA

Fig. 9C

AAATCCGCAGGAAAAACTGCCCGGCGTGTCGCCTTAGAAAGTGCTGTCAAGCTGGCATGGTCCT

TGGAGGGCGAAAGTTTAAAAAGTTCAATAAAGTCAGAGTCATGAGAGCACTCGATGCTGTTGCT

CTCCCACAGCCAGTGGGCATTCCAAATGAAAGCCAACGAATCACTTTTTCTCCAAGTCAAGAGA

TACAGTTAATTCCCCCTCTAATCAACCTGTTAATGAGCATTGAACCAGATGTGATCTATGCAGG

ACATGACAACACAAAGCCTGATACCTCCAGTTCTTTGCTGACGAGTCTTAATCAACTAGGCGAG

CGGCAACTTCTTTCAGTGGTAAAATGGTCCAAATCTCTTCCAGGTTTTCGAAACTTACATATTG

ATGACCAGATAACTCTCATCCAGTATTCTTGGATGAGTTTAATGGTATTTGGACTAGGATGGAG

ATCCTACAAACATGTCAGTGGGCAGATGCTGTATTTTGCACCTGATCTAATATTAAATGAACAG

CGGATGAAAGAATCATCATTCTATTCACTATGCCTTACCATGTGGCAGATACCGCAGGAGTTTG

TCAAGCTTCAAGTTAGCCAAGAAGAGTTCCTCTGCATGAAAGTATTACTACTTCTTAATACAAT

TCCTTTGGAAGGACTAAGAAGTCAAAGCCAGTTTGAAGAGATGAGATCAAGCTACATTAGAGAG

CTCATCAAGGCAATTGGTTTGAGGCAAAAAGGAGTTGTTTCCAGCTCACAGCGTTTCTATCAGC

TCACAAAACTTCTTGATAACTTGCATGATCTTGTCAAACAACTTCACCTGTACTGCCTGAATAC

Fig. 9D

ATTTATCCAGTCCCGGGCGCTGAGTGTTGAATTTCCAGAAATGATGTCTGAAGTTATTGCTGCA

CAGTTACCCAAGATATTGGCAGGGATGGTGAAACCACTTCTCTTTCATAAAAAGTGAATGTCAA

TTATTTTTCAAAGAATTAAGTGTTGTGGTATGTCTTTCGTTTTGGTCAGGATTATGACGTCTCG

AGTTTTTATAATATTCTGAAAGGGAATTCCTGCAGCCCGGGGGATCCACTAGTTCTAGAGGATC

CAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATG

CTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAATAAACAA

GTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGGTGTGGGAGGTTTTTT

AAAGCAAGTAAAACCTCTACAAATGTGGTATGGCTGATTATGATCCTGCAAGCCTCGTCGTCTG

GCCGGACCACGCTATCTGTGCAAGGTCCCCGGACGCGCTCCATGAGCAGAGCGCCCGCCGCC

GAGGCAAGACTCGGGCGGCGCCCTGCCCGTCCCACCAGGTCAACAGGCGGTAACCGGCCTCTTC

ATCGGGAATGCGCGCGACCTTCAGCATCGCCGGCATGTCCCCTGGCGGACGGGAAGTATCAGCT

CGACCAAGCTTGGCGAGATTTTCAGGAGCTAAGGAAGCTAAAATGGAGAAAAAAATCACTGGAT

ATACCACCGTTGATATATCCCAATGGCATCGTAAAGAACATTTTGAGGCATTTCAGTCAGTTGC

Fig. 9E

TCAATGTACCTATAACCAGACCGTTCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGC

GGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGC

TGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAA

CGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTG

CTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGA

GGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCG

CTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG

GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGG

GCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGA

GTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGA

GCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAA

GGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTC

TTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACG

Fig. 9F

CGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGA

ACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCT

TTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT

TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTG

CCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGC

AATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGA

AGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCC

GGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGG

CATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGG

CGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTG

TCAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTAC

TGTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAA

TAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATA

Fig. 9G

GCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTT

ACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTT

ACTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAA

GGGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCA

GGGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTT

CCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTCTAAGAAACCATTATTATCATGACATTAA

CCTATAAAAATAGGCGTATCACGAGGCCCTTTCGTC

Fig. 9H

CTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATC

AGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGT

CGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAG

TGATAGAGAAAAGTGAAAGTCGAGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCG

AGTTTACCACTCCCTATCAGTGATAGAGAAAAGTGAAAGTCGAGCTCGGTACCCGGGTCGAGTA

GGCGTGTACGGTGGGAGGCCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCCTGGAG

ACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGCGGCCCC

GAATTCCGCCCACGACCATGACCATGACCCTCCACACCAAAGCATCTGGGATGGCCCTACTGCA

TCAGATCCAAGGGAACGAGCTGGAGCCCCTGAACCGTCCGCAGCTCAAGATCCCCCTGGAGCGG

CCCCTGGGCGAGGTGTACCTGGACAGCAGCAAGCCCGCCGTGTACAACTACCCCGAGGGCGCCG

CCTACGAGTTCAACGCCGCGGCCGCCGCCAACGCGCAGGTCTACGGTCAGACCGGCCTCCCCTA

CGGCCCCGGGTCTGAGGCTGCGGCGTTCGGCTCCAACGGCCTGGGGGGTTTCCCCCCACTCAAC

AGCGTGTCTCCGAGCCCGCTGATGCTACTGCACCCGCCGCCGCAGCTGTCGCCTTTCCTGCAGC

Fig. 10A

CCCACGGCCAGCAGGTGCCCTACTACCTGGAGAACGAGCCCAGCGGCTACACGGTGCGCGAGGC

CGGCCCGCCGGCATTCTACAGGCCAAATTCAGATAATCGACGCCAGGGTGGCAGAGAAAGATTG

GCCAGTACCAATGACAAGGGAAGTATGGCTATGGAATCTGCCAAGGAGACTCGCTACTGTGCAG

TGTGCAATGACTATGCTTCAGGCTACCATTATGGAGTCTGGTCCTGTGAGGGCTGCAAGGCCTT

CTTCAAGAGAAGTATTCAAGGACATAACGACTATATGTGTCCAGCCACCAACCAGTGCACCATT

GATAAAAACAGGAGGAAGAGCTGCCAGGCCTGCCGGCTCCGCAAATGCTACGAAGTGGGAATGA

TGAAAGGTGGGATACGAAAAGACCGAAGAGGAGGGAGAATGTTGAAACACAAGCGCCAGAGAGA

TGATGGGGAGGGCAGGGGTGAAGTGGGGTCTGCTGGAGACATGAGAGCTGCCAACCTTTGGCCA

AGCCCGCTCATGATCAAACGCTCTAAGAAGAACAGCCTGGCCTTGTCCCTGACGGCCGACCAGA

TGGTCATGGCCTTGTTGGATGCTGAGCCCCCCATACTCTATTCCGAGTATGATCCTACCAGACC

CTTCAGTGAAGCTTCGATGATGGGCTTACTGACCAACCTGGCAGACAGGGAGCTGGTTCACATG

ATCAACTGGGCGAAGAGGGTGCCAGGCTTTGTGGATTTGACCCTCCATGATCAGGTCCACCTTC

TAGAATGTGCCTGGCTAGAGATCCTGATGATTGGTCTCGTCTGGCGCTCCATGGAGCACCCAGT

Fig. 10B

GAAGCTACTGTTTGCTCCTAACTTGCTCTTGGACAGGAACCAGGGAAAATGTGTAGAGGGCATG

GTGGAGATCTTCGACATGCTGCTGGCTACATCATCTCGGTTCCGCATGATGAATCTGCAGGGAG

AGGAGTTTGTGTGCCTCAAATCTATTATTTTGCTTAATTCTGGAGTGTACACATTTCTGTCCAG

CACCCTGAAGTCTCTGGAAGAGAAGGACCATATCCACCGAGTCCTGGACAAGATCACAGACACT

TTGATCCACCTGATGGCCAAGGCAGGCCTGACCCTGCAGCAGCAGCACCAGCGGCTGGCCCAGC

TCCTCCTCATCCTCTCCCACATCAGGCACATGAGTAACAAAGGCATGGAGCATCTGTACAGCAT

GAAGTGCAAGAACGTGGTGCCCCTCTATGACCTGCTGCTGGAGATGCTGGACGCCCACCGCCTA

CATGCGCCCACTAGCCGTGGAGGGGCATCCGTGGAGGAGACGGACCAAAGCCACTTGGCCACTG

CGGGCTCTACTTCATCGCATTCCTTGCAAAAGTATTACATCACGGGGGAGGCAGAGGGTTTCCC

TGCCACAGTCTGAGAGCTCCCTGGCGGAATTCGAGCTCGGTACCCGGGGATCCTCTAGAGGATC

CAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATG

CTTTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAATAAACAA

GTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGGTGTGGGAGGTTTTTT

Fig. 10C

AAAGCAAGTAAAACCTCTACAAATGTGGTATGGCTGATTATGATCCTGCAAGCCTCGTCGTCTG

GCCGGACCACGCTATCTGTGCAAGGTCCCCGGACGCGCTCCATGAGCAGAGCGCCCGCCGCC

GAGGCAAGACTCGGGCGGCGCCCTGCCCGTCCCACCAGGTCAACAGGCGGTAACCGGCCTCTTC

ATCGGGAATGCGCGCGACCTTCAGCATCGCCGGCATGTCCCCTGGCGGACGGGAAGTATCAGCT

CGACCAAGCTTGGCGAGATTTTCAGGAGCTAAGGAAGCTAAAATGGAGAAAAAAATCACTGGAT

ATACCACCGTTGATATATCCCAATGGCATCGTAAAGAACATTTTGAGGCATTTCAGTCAGTTGC

TCAATGTACCTATAACCAGACCGTTCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGC

GGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGC

TGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAA

CGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTG

CTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGA

GGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCG

CTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTG

Fig. 10D

GCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGG

GCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGA

GTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGA

GCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAA

GGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTC

TTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACG

CGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGA

ACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCT

TTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGT

TACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTG

CCTGATCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCA

ATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAA

GGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCG

Fig. 10E

GGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTGCGCAACGTTGTTGCCATTGCTACAGGC

ATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCAACGATCAAGGC

GAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGT

CAGAAGTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACT

GTCATGCCATCCGTAAGATGCTTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAAT

AGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTCAATACGGGATAATACCGCGCCACATAG

CAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCTCAAGGATCTTA

CCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTA

CTTTCACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAG

GGCGACACGGAAATGTTGAATACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAG

GGTTATTGTCTCATGAGCGGATACATATTTGAATGTATTTAGAAAAATAAACAAATAGGGGTTC

CGCGCACATTTCCCCGAAAAGTGCCACCTGACGTCTAAGAAACCATTATTATCATGACATTAAC

CTATAAAAATAGGCGTATCACGAGGCCCTTTCGTC

Fig. 10F

FIG.11

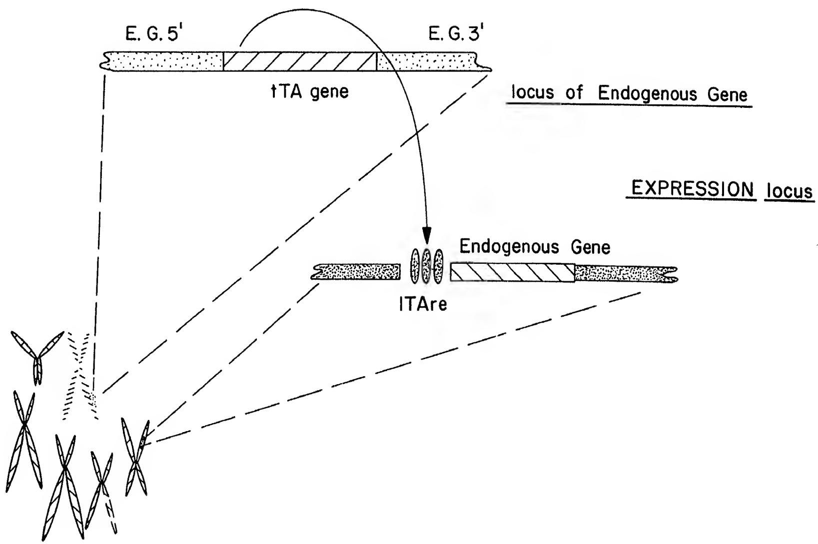

E. G. 5'
E. G. 3'
tTA gene
locus of Endogenous Gene
EXPRESSION locus
Endogenous Gene
lTAre

FIG. 12

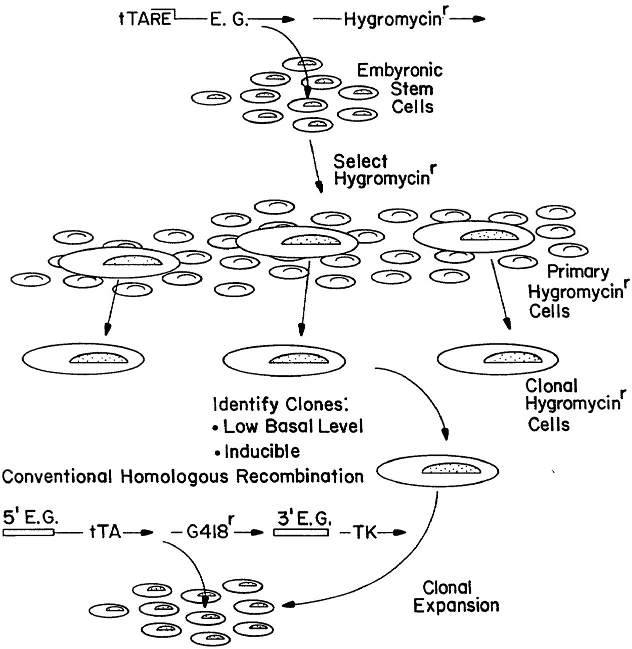

tTARE
E. G.
Hygromycin^r
Embryonic Stem Cells
Select Hygromycin^r
Primary Hygromycin^r Cells
Clonal Hygromycin^r Cells
Identify Clones:
• Low Basal Level
• Inducible
Conventional Homologous Recombination
5' E.G.
tTA
G418^r
3' E.G.
TK
Clonal Expansion

FIG. 13A

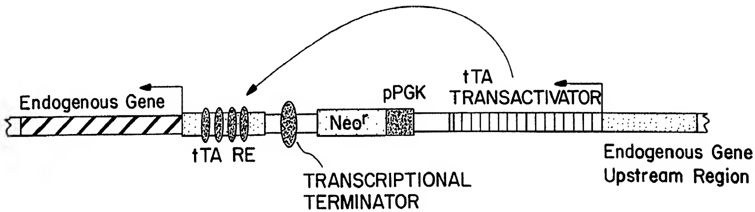


FIG. 13B

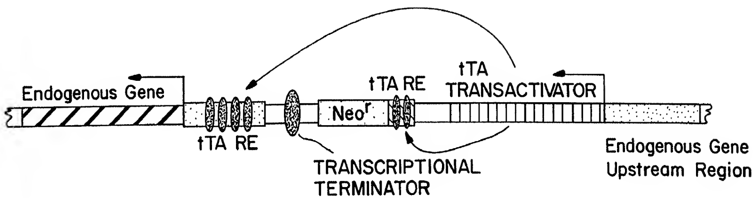
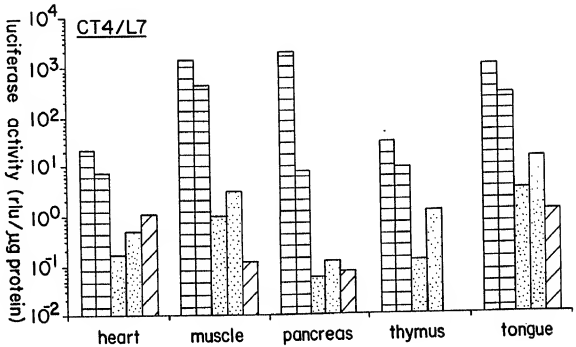


FIG.14


CT4/L7
10^4
10^3
10^2
10^1
10^0
10^{-1}
10^{-2}
luciferase activity (rlu/µg protein)
heart
muscle
pancreas
thymus
tongue